

Remarks

The August 18, 2005 Official Action has been carefully reviewed. In view of the amendments submitted herewith and the following remarks, favorable reconsideration and allowance of this application are respectfully requested.

At the outset it is noted that a shortened statutory response period of three (3) months was set forth in the August 18, 2005 Official Action. Therefore, the initial due date for response is November 18, 2005.

At page 2 of the Official Action, the Examiner states that instant application fails to comply with the requirements of 37 CFR §§1.821-1.825. Specifically, the Examiner asserts that the *scbA* and *scbR* genes from *S. coelicolor* presented in the specification at page 4, lines 13 and 35; page 5, line 21; page 6, line 24; page 7, lines 27-30; and the figure descriptions of Figures 4b and 9-14, require sequence identifiers. Additionally, the Examiner point out that there are nucleotide sequences at page 11, line 35 through page 12, line 27 and at pages 34-39 without sequence identifiers.

Applicants respectfully disagree with the Examiner's position. At the outset, Applicants filed an Amendment with the Sequence Listing on January 5, 2004. The January 5, 2004 Amendment inserted sequence identifiers, where required, from page 11, line 28 through page 12, line 32, into the figure descriptions for Figures 4b, 9-11, and 14; and from page 34, line 8 through page 40, line 12. Accordingly, Applicants respectfully submit that the Examiner's objection to the specification at these locations for lacking sequence identifiers is improper and Applicants respectfully request their withdrawal.

Additionally, Applicants respectfully disagree with the Examiner's contention that sequence identifiers need to be inserted at page 4, lines 13 and 35; page 5, line 21; page 6, line 24; and in the figure descriptions of Figures 12 and 13.

Applicants submit that page 4, lines 13 and 35; page 5, line 21; and page 6, line 24 generally refer to the scbA and the scbR genes. Further, Figures 12 and 13 are graphs of the production of Act and Red, respectively. Figures 12 and 13 and their figure descriptions do not contain any nucleotide or amino acid sequences. Accordingly, Applicants submit that it would be unnecessary and improper to restrict the instant specification to the specifically disclosed nucleotide sequences. Indeed, 37 CFR §1.821(d) states that "[w]here the description or claims of a patent application discuss a **sequence** that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier." [Emphasis added.] Applicants submit that the specification at the above cited passages only discuss the genes in general and do not specifically "discuss a sequence," as required by 37 CFR §1.821(d).

Inasmuch as the specification at page 7, lines 27-30 does refer to the specific sequences provided in Figures 9-11, Applicants have inserted appropriate sequence identifiers.

In light of all of the foregoing, Applicants respectfully submit that the Examiner's objection to the specification for allegedly failing to satisfy the sequence requirements set forth in 37 CFR §§1.821-1.825 is untenable. Accordingly, Applicants respectfully request the objections be withdrawn.

The Examiner has also objected to claims 15 and 20. Specifically, the Examiner has objected to the symbol "©" in claim 15 and objected to claim 20 for depending from cancelled claim 19. Applicants have amended claim 15 to delete the symbol "©" and have amended claim 20 to depend from currently pending claim 15. Accordingly, Applicants submit that the Examiner's objections to claims 15 and 20 have been rendered moot and respectfully request their withdrawal.

Claims 1, 9, 11, 13, 15, and 20-23 have been

rejected under 35 U.S.C. §112, second paragraph for alleged indefiniteness.

Claims 1, 9, 11, 13, and 15 have also been rejected for allegedly failing to satisfy the written description requirement of 35 U.S.C. §112, first paragraph.

Lastly, the Examiner has rejected claims 15 and 20-23 for allegedly failing to satisfy the enablement requirement of 35 U.S.C. §112, first paragraph.

The foregoing objections and rejections constitute all of the grounds set forth in the August 18, 2005 Official Action for refusing the present application.

In accordance with this amendment, claims 1, 9, 15, and 20 have been amended. Claim 20 has been amended to properly depend from claim 15 instead of cancelled claim 19. Support for the amendments to claims 1, 9, and 15 can be found throughout the specification including, for example, at page 12, lines 4-11 and page 20, line 27.

No new matter has been introduced into this application by reason of any of the amendments presented herewith.

In view of the present amendment and the reasons set forth in this response, Applicants respectfully submit that the objection to the specification; the objection to claims 15 and 20; the 35 U.S.C. §112, first paragraph rejections of claims 1, 9, 11, 13, 15, and 20-23; and the 35 U.S.C. §112, second paragraph rejections of claims 1, 9, 11, 13, 15, and 20-23, as set forth in the August 18, 2005 Official Action, cannot be maintained. These grounds of objection and rejection are, therefore, respectfully traversed.

CLAIMS 1, 9, 11, 13, 15, AND 20-23, AS AMENDED, MEET THE REQUIREMENTS UNDER 35 U.S.C. §112, SECOND PARAGRAPH

The Examiner has rejected claims 1, 9, 11, 13, 15, and 20-23 under 35 U.S.C. §112, second paragraph for alleged indefiniteness on the following two grounds.

First, it is the Examiner's position that claims 1, 9, and 15 are indefinite for the recitation of "scbA gene," without being identified with a sequence identifier.

Applicants respectfully disagree with the Examiner. However, in the interest of expediting prosecution of the instant application, Applicants have amended claims 1, 9, and 15, from which claims 11, 13, and 20-23 depend, to recite that the scbA gene encodes a polypeptide of SEQ ID NO: 17. Accordingly, Applicants respectfully submit that the instant rejection has been overcome.

Second, the Examiner contends that the metes and bounds of the phrase "capable of specific hybridization" in claim 15 are unclear. Applicants have amended claim 15 to eliminate the allegedly ambiguous phrase, thereby rendering the instant rejection moot.

In light of the foregoing, Applicants submit that the rejections of claims 1, 9, 11, 13, 15, and 20-23 under 35 U.S.C. §112, second paragraph for alleged indefiniteness are untenable and respectfully request their withdrawal.

CLAIMS 1, 9, 11, 13, AND 15, AS AMENDED, SATISFY THE WRITTEN DESCRIPTION REQUIREMENT UNDER 35 U.S.C. §112, FIRST PARAGRAPH

The Examiner has rejected claims 1, 9, 11, 13, and 15 for allegedly failing to satisfy the written description requirement of 35 U.S.C. §112, first paragraph on the following three grounds.

First, it is the Examiner's position that item (c) of claim 15 is new matter. Applicants respectfully disagree, given that page 11, line 33 to page 12, line 3 provides support for item (c) of claim 15. However, in the sole interest of expediting prosecution of the instant application, Applicants have deleted item (c) from claim 15, thereby rendering the instant rejection moot.

Second, the Examiner contends that the specification fails to provide support for the phrase "species being other

than ... *S. griseus*" recited in claim 15. Applicants respectfully disagree. Claim 15 is generally drawn to a method for identifying *Streptomyces* species in which antibiotic production would be **increased** by functional deletion of the *scbA* gene or a homolog thereof. The specification clearly discloses, however, that the functional deletion of *asfA*, the *S. griseus* homolog of *scbA*, results in a **deficiency** of streptomycin production (see, e.g., page 2, lines 17-19; page 4, 18-19; page 5, lines 11-13; page 32, lines 21-24; and page 33, lines 6-18). Accordingly, Applicants submit that the specification provides clear support for the method of claim 15 which encompasses species other than *S. griseus*.

Third, it is the Examiner's position that the specification has failed to provide a representative number of species to claim the genus of *scbA* genes as recited in claims 1, 9, 11, and 13. For the reasons set forth hereinabove, Applicants have amended claims 1 and 9, from which claims 11 and 13 depend, to recite that the *scbA* gene encodes a polypeptide having the sequence of SEQ ID NO: 17. As suggested by the Examiner at page 4 of the instant Official Action, the recitation of the specific amino acid sequence overcomes the instant rejection.

In view of the foregoing, Applicants submit that the Examiner's rejections of claims 1, 9, 11, 13, and 15 for allegedly failing to satisfy the written description requirement of 35 U.S.C. §112, first paragraph are untenable and respectfully request their withdrawal.

**CLAIMS 15 AND 20-23 SATISFY THE ENABLEMENT REQUIREMENT UNDER
35 U.S.C. §112, FIRST PARAGRAPH**

The Examiner has rejected claims 15 and 20-23 for allegedly failing to satisfy the enablement requirement of 35 U.S.C. §112, first paragraph. Specifically, it is the

Examiner's position that the identifying of an scbA gene homolog in any Streptomyces "wherein the gene product has 35%, 50%, 65% and 80% amino acid homology to SEQ ID NO: 17," disabling the identified gene, and ascertaining the effects of the disablement of the gene is "outside the realm of routine experimentation."

The MPEP at §2164.01 clearly states that the "fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue."

Applicants respectfully disagree with the Examiner's position. At the outset, Applicants note that the Examiner has only expressly indicated that gene products having "35%, 50%, 65% and 80% amino acid homology to SEQ ID NO: 17" present an enablement issue. Notably, claim 23 recites that the gene product has 95% homology to SEQ ID NO: 17. Accordingly, Applicants submit that claim 23 has been erroneously included in the instant rejection.

The Examiner also states at page 5 of the instant Official Action that the "amount of experimentation to identify scbA gene is enormous" and that "a gene could not be disabled by known methods, unless the [person of] ordinary skill in the art knows the gene." Applicants respectfully disagree with the Examiner. Example 8 (pages 29-41) of the instant application clearly demonstrates that the scbA gene sequence information (SEQ ID NO: 19) can be used to functionally delete the coding sequence of a similar gene in another species, even without knowing the sequence of the gene in that species. Indeed, it is demonstrated in Example 8 that a mutant scbA allele from *S. coelicolor* can be introduced into *S. lividans* and that the allele becomes integrated into the chromosomal DNA (page 29, lines 24-26). Routine PCR analysis and restriction digest analysis of the chromosomal DNA

revealed the integration of the mutant scbA allele (page 29, line 32 to page 30, line 7). Furthermore, it is demonstrated at page 29, line 8 through page 31, line 10, that the transformed cells did not express scbA and that antibiotic synthesis was "precocious and elevated." Accordingly, Applicants submit that the instant application provides more than adequate guidance to the skilled artisan for mutating a structurally similar gene by, for example, homologous recombination.

The Examiner also states that the skilled artisan, in order to practice the instantly claimed invention, would require the additional guidance of which antibiotics are enhanced upon the disablement of scbA. Applicants respectfully disagree inasmuch as it is a routine matter to determine whether the production of an antibiotic is affected in a given strain by the mutation of a gene. Most, if not all, Streptomyces strains make secondary metabolites of which many are antibiotics. For a number of Streptomyces strains, the antibiotics produced have already been discovered. For newly characterized strains, the antibiotics produced can be determined using routine screening techniques. It is also a routine matter for a skilled artisan to determine whether the mutation of the gene results in increased production of the antibiotic, as exemplified in Example 8 for the antibiotics Act and Red.

Accordingly, Applicants submit that the skilled artisan, when presented with the sequence and functional information and the guidance provided in the present application, is fully capable of practicing the invention as instantly claimed, using routine techniques known in the art and without undue experimentation.

In light of the foregoing, Applicants respectfully submit that the instant rejection of claims 15 and 20-23 for allegedly failing to satisfy the enablement requirement of 35 U.S.C. §112, first paragraph is untenable. Applicants

respectfully request the withdrawal of the instant rejection.

CONCLUSION

In view of the amendments presented herewith and the foregoing remarks, it is respectfully urged that the objections and rejections set forth in the August 18, 2005 Official Action be withdrawn and that this application be passed to issue.

In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, the Examiner is requested to telephone the undersigned attorney at the phone number give below.

Respectfully submitted,
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